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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/512,731	10/26/2004	Daniel W. Chan	57222(71699)	1716

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/512,731	CHAN ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,30,31,42 and 43* is/are pending in the application.

4a) Of the above claim(s) *6-10, 30, 31, 42, and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 11, and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 October 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20050411*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The election without traverse filed April 27, 2007, is acknowledged and has been entered.

Applicant has elected the invention of Group II, claim 5, insofar as the claim is drawn to a method of qualifying prostate cancer status in a subject, said method comprising measuring at least one biomarker in a sample from the subject, wherein said prostate cancer status is the type of disease

Claims 1-4, 11, and 12 are linking claims, linking the inventions of Groups I, II, III, and IV.

Applicant has further elected the species of the invention of Group III, wherein the at least one biomarker is "Marker I" having a molecular weight of about 7.808 kD.

Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-12, 30, 31, 42, and 43 are pending in the application. Claims 6-10, 30, 31, 42, and 43 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 27, 2007.

3. Claims 1-5, 11, and 12 are currently under prosecution.

Information Disclosure Statement

4. The information disclosure filed April 11, 2005, has been considered. An initialed copy is enclosed.

Priority

5. Applicant's claim under 35 U.S.C. §§ 119 and/or 120 for benefit of the earlier filing date of PCT Application No. PCT/US03/12729, filed April 25, 2003, which claims benefit of U.S. Provisional Application No. 60/375,719, filed April 26, 2002, is acknowledged.

However, claims 1-5, 11, and 12 do not properly benefit under §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and/or a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In addition, it is aptly noted that claims 1-5, 11, and 12 would not properly benefit under §§ 119 and/or 120 by the earlier filing date of the provisional application because it does not provide written support for the claimed process of "qualifying prostate cancer status in a subject". The provisional application does not, for example, describe "qualifying prostate cancer status" by means of determining the subject's risk of cancer or the type of disease; and, at best, it would only serve to provide support for a method for aiding in the diagnosis of prostate cancer by permitting one to distinguish between samples acquired from subject's afflicted with prostate cancer and samples acquired from unaffected subject's.

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely October 26, 2004.

Specification

6. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of such an improperly demarcated trademark appearing in the specification is Proteinchip™; see, e.g., page 3, line 25.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

Claim Objections

7. Claims 1-5, 11, and 12 are objected to as being directed to the subject matter of non-elected inventions.

Appropriate correction is required.

8. Claims 1-5, 11, and 12 are objected to as being directed to the subject matter of non-elected species of the invention of Group III.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5, 11, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-5, 11, and 12 are indefinite for the following reason:

Claim 1-5, 11, and 12 are directed to a method for qualifying "prostate cancer status" in a subject, wherein, as recited in claim 5, said "prostate cancer status" is "the type of disease"; yet, the claim merely recites an active process comprising measuring at least one biomarker in a sample from the subject and correlating the measurement with "the type of the disease". How is the measurement correlated with "the type of the disease"? None of the claims clearly and particularly point out the actual process steps by which "the type of the disease" is qualified. Therefore, it is submitted that there is no process step that clearly relates back to the different purposes or objectives of the claimed invention; and consequently, the skilled artisan would not know, and could not determine whether each and every process step considered essential to the practice of the claimed invention has been included in the body of the claim. Thus, in the absence of a correlative step positively relating the whole of the process to its intended uses, as recited in the preamble, the claim fails to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(b) Claim is 4 is indefinite for the following reason:

Claim 4 recites, "further comprising: (d) measuring the at least one biomarker after subject treatment". Claim 4 depends from claim 2, which is directed to the method of claim 1, wherein the method further comprises "managing subject treatment" based on the status. According to claim 3, "managing subject treatment" is selected from "ordering more tests", "performing surgery", and "taking no further action". If during the practice of the invention of claim 4 the practitioner selected to manage subject treatment by "taking no further action" it cannot be known or determined when the at least one biomarker is necessarily measured afterward. Accordingly, the claim fails to delineate the metes and bounds of the subject matter that is regarded as the invention with the clarity and particularity necessary to satisfy the

requirement set forth under 35 U.S.C. § 112, second paragraph, so as to permit the skilled artisan to know or determine infringing subject matter.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-5, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** any process encompassed by the claims, which has been disclosed by the prior art, **does not reasonably provide enablement for using** the claimed processes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim 1-5, 11, and 12 are directed to a method for qualifying the type of disease in a subject; yet, the claims merely recite an active process comprising measuring at least one biomarker in a sample from the subject and correlating the measurement with the type of the disease. The claims do not recite any particular active process step by which the measurement made (i.e., presumably the quantity of the biomarker) is correlated with the type of the disease in the subject. It appears therefore that each and every process step considered essential to the practice of the claimed invention has not been included in the body of the claim. Consequently, the skilled artisan would not know how the claimed invention is to be used to achieve the claimed objective of qualifying the type of disease in the subject.

In addition, it is aptly noted that the specification teaches only an apparent association between an abnormal level of a biomarker having the molecular weight of about 7.808 kDa in the serum of subjects and the presence of a disease, namely prostate cancer in those subjects. More particularly, the specification teaches that the level of a marker of about 7.808 kDa is down-regulated in serum samples acquired from men afflicted with prostate cancer, as compared to its level in serum samples acquired from healthy men; see, e.g., "Panel 1" at page 64 of the specification. The specification does not teach any association between the presence of the biomarker and the type of the disease.

It is submitted for these reasons that the amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed to qualify the type of disease in a subject without undue and/or unreasonable experimentation.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-5, 11, and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Tsuneki et al. (*BMC Pharmacol.* 2004 Aug 26; **4**: 18; copy of on-line publication; pp. 1-10).

Claims 1-5, 11, and 12 are drawn to a process of qualifying the type of disease in a subject, said process comprising measuring at least one biomarker in a sample from the subject, wherein the at least one biomarker has a molecular weight of about 7.808 kDa and correlating the measurement with the type of disease (claims 1-5), wherein the marker is detected by mass spectrometry (claim 11) or wherein the marker is detected by capturing the marker on a biochip having an affinity surface and detecting the captured marker by SELDI (claim 12). Although claims 2-4 are directed to the process of claim 1, further comprising managing subject treatment based on the status (i.e., type of disease), according to claim 3, "managing subject treatment" includes "taking no further action".

Tsuneki et al. teaches a process comprising measuring at least one biomarker in a sample from a subject, wherein at least one biomarker has a molecular weight of about 7.808 kDa and correlating the measurement with the type of disease; see entire document (e.g., the abstract). Tsuneki et al. teaches the level of the marker is determined upon its detection by mass spectrometry, or more particularly SELDI; see, e.g., the abstract.

15. Claims 1-5, 11, and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Gretzer et al. (*Prostate*. 2004 Sep 1; **60** (4): 325-331).

The claims are drawn to a process comprising detecting and measuring the level of at least one biomarker in a sample from a subject and correlating the measurement with the type of disease, wherein the at least one biomarker is "Marker I", a biomarker having a molecular weight of about 7.808 kDa.

With regard to the term "about", M.P.E.P. § 2173.05(b) states: "The Court held that claims reciting "at least about" were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term "about." *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)".

With regard to the term "about", as it is used in the claims to define the molecular weights of the biomarkers to which the claims are directed, at paragraph [0017] of the published application[1], the specification discloses the following:

> For the mass values of the markers disclosed herein, the mass accuracy of the spectral instrument is considered to be about within +/-0.15 percent of the disclosed molecular weight value. Additionally, to such recognized accuracy variations of the instrument, the spectral mass determination can vary within resolution limits of from about 400 to 1000 m/dm, where m is mass and dm is the mass spectral peak width at 0.5 peak height. Those mass accuracy and resolution variances associated with the mass spectral instrument and operation thereof are reflected in the use of the term "about" in the disclosure of the mass of each of Markers I through XXXII. It is also intended that such mass accuracy and resolution variances and thus meaning of the term "about" with respect to the mass of each of the markers disclosed herein is inclusive of variants of the markers as may exist due to sex, genotype and/or ethnicity of the subject and the particular cancer or origin or stage thereof.

Gretzer et al. teaches a process comprising detecting and measuring the level of at least one biomarker in a sample from a subject, wherein the at least one biomarker is a biomarker having a molecular weight of *about* 7.808 kDa (e.g., 9 kDa) and correlating the measurement with the type of disease in the subject; see entire document (e.g., the abstract; and page 330, column 1). More particularly, Gretzer et al. teaches samples were acquired from subjects, which were used to establish different cell lines having varying mestastatic potential; see, e.g., the abstract. Gretzer et al. teaches detecting and measuring the level of the markers in lysates of the cultured cell lines; see, e.g., page 327, column 1. Gretzer et al. teaches the detection and

[1] U.S. Patent Application Publication No. 2005/0176011 A1.

measurement was made using a ProteinChip™ SELDI immunoassay, a mass spectrometry-based technique; see, e.g., the abstract; and page 327, column 2,through page 328, column 1.

16. Claims 1-5, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Cazares et al. (*Clin. Cancer Res.* 2002 Aug; **8** (8): 2541-2552).

The claims are drawn to a process comprising detecting and measuring the level of at least one biomarker in a sample from a subject and correlating the measurement with the type of disease, wherein the at least one biomarker is "Marker I", a biomarker having a molecular weight of about 7.808 kDa.

Cazares et al. teaches a process comprising detecting and measuring the level of at least one biomarker in a sample from a subject, wherein the at least one biomarker is a biomarker having a molecular weight of *about* 7.808 kDa; see entire document (e.g., the abstract; page 2544, Figure 1A). More particularly, Cazares et al. teaches the detection and measurement of biomarkers in matched tissue samples acquired from patients before surgery or from subjects not affected by the disease, which have molecular weights of approximately 6,913, 7,368, and 8238 kDa, or *about* 7.808 kDa (page 2544, Figure 1A). Cazares et al. teaches the detection and measurement was made using a ProteinChip™ SELDI immunoassay, a mass spectrometry-based technique; see, e.g., page 2542, column 2, through page 2543, column 1). Cazares et al. teaches correlating the measurements with the type of disease; see, e.g., the abstract.

Conclusion

17. No claim is allowed.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Shah et al. (*Cancer Res.* 2004 Dec 15; **64** (24): 9209-9216) teaches metastatic hormone-refractory prostate cancer has a heterogeneous morphology, immunophenotype, and genotype, demonstrating that "metastatic disease" is a group of diseases even within the same patient. Lapointe et al. (*Proc. Natl. Acad. Sci U S A.* 2004 Jan 20; **101** (3): 811-816) teaches gene expression profiling identifies clinically relevant subtypes of prostate cancer.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner
Art Unit 1643

slr
July 8, 2007